Extended Anticoagulant Treatment with Full- or Reduced-Dose Apixaban in Patients with Cancer-Associated Venous Thromboembolism: Rationale and Design of the API-CAT Study

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Background

- Venous thromboembolism (VTE) is a common complication of cancer, and is associated with a high risk of recurrence.
- Current guidelines suggest continuing anticoagulant therapy with no scheduled stop date as long as the cancer is active and/or anticancer treatment is ongoing with a substantial risk of bleeding.
- The results of the AMPLIFY extension study, showing promising results of the apixaban 2.5 mg dosage, compared with the 5 mg dosage, in terms of recurrence and major bleedings, and the reassuring data in the subgroup of patients with cancer, have led to consider the opportunity to test the 2.5 mg bid dosage against the 5 mg bid dosage, after completing the first 6 months of treatment, in a wide population of cancer patients.

AIM of the study

- The aim of the API-CAT study is to assess whether a reduced dose regimen of apixaban (2.5 mg bid) is noninferior to a full dose regimen of apixaban (5mg bid) for the prevention of recurrent VTE in patients with active cancer who have completed at least 6 months of anticoagulant therapy for treating a documented index event of proximal DVT or PE.
- The key secondary objective is to assess whether a reduced dose regimen of apixaban (2.5 mg bid) is safer than a full dose regimen of apixaban (5 mg bid) in terms of clinically relevant bleeding.

Methods (I)

- API-CAT (NCT03692065) is an international, prospective, randomized, parallel-group, double-blind, double-dummy, non inferiority clinical trial with blinded adjudication of outcome events.
- The study is planned to be conducted in approximately 160 centers in 11 countries.
- Patients with active cancer who have completed at least 6 months of anticoagulant therapy (with a LMWH, DOAC, or vitamin K antagonist) for the treatment of an objectively proven symptomatic or incidental VTE are eligible for enrolment in the study.
- Patients are randomized in a double-blind fashion (1:1 ratio) to receive either a reduced-dose regimen of apixaban(2.5 mg bid) or a full-dose regimen of apixaban (5 mg bid) for 12 months.

Methods (II)

- The study requires the following scheduled visits: enrolment, 1 month, 3 months, 6 months, 9 months, 12 months, and 13 months after randomization. Additional visits are performed if new symptoms and/or signs of VTE occur during the study period.
- The primary efficacy outcome is a composite of adjudicated recurrent symptomatic or incidental VTE, or death due to PE during the 12-month treatment period.
- The key secondary outcome is a composite of adjudicated major or clinically relevant nonmajor bleeding during the 12-month treatment period.
- Other outcomes are recurrent symptomatic VTE, VTE related-death, all-cause death, major bleeding, and the composite of recurrent symptomatic VTE, VTE-related death, all cause death, or major bleeding.

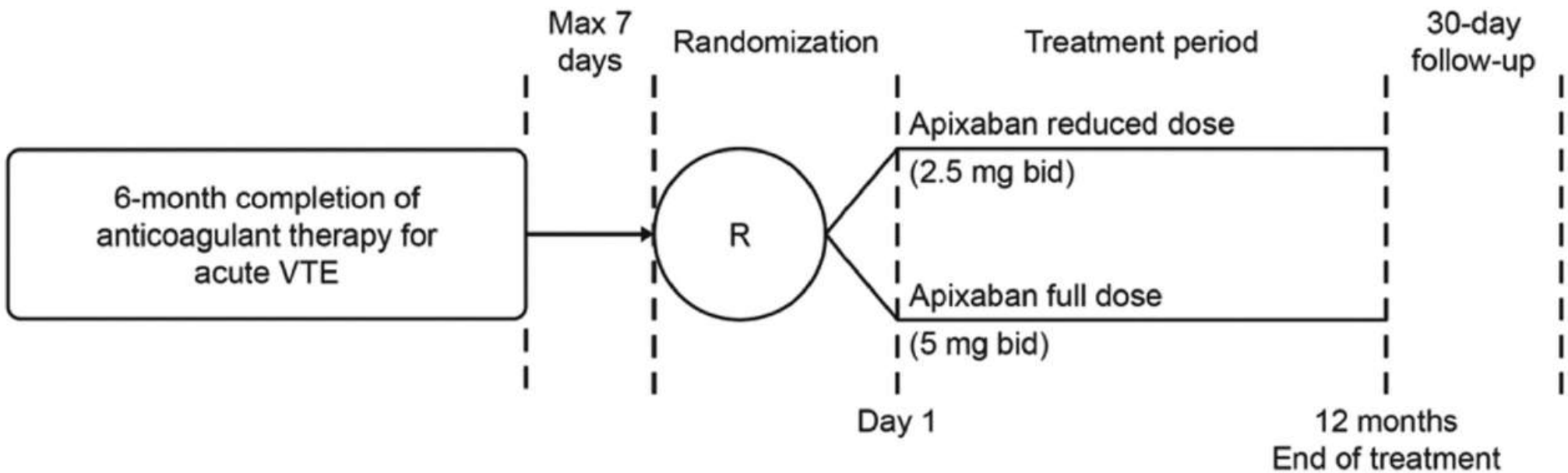

Fig. 1 Design of the randomized, double-blind, noninferiority API-CAT study. bid, twice daily; Max, maximum; mo., months; R, randomization; VTE, venous thromboembolism.

Table 3 Flowchart/patient follow-up summary and distinction between procedures associated with usual care and procedures performed because of the API-CAT study protocol

	Baseline visit[a]	Week 4[b] ± 15 days	Month 3 ± 15 days	Month 6 ± 15 days	Month 9 ± 15 days	Month 12 (end of treatment visit ± 15 days	Month 13 (30-day posttreatment visit ± 15 days
Informed consent[c]	X						
Inclusion/exclusion criteria[c]	X						
Randomization[c]	X						
Medical history[c]	X						
Physical examination	X	x	x	x	x	x	
Height, weight	X						
Vital signs	X	x	x	x	x	x	
Documentation of index event	X						
Adverse event assessment[c]		x	x	x	x	x	x
Outcome assessment[c]		x	x	x	x	x	x
Clinical laboratory tests[d]	x	X	x	x	x	x	
Urinary pregnancy test[c]	x	X	x	x	x	x	
Assess medication use[c]		X	x	x	x	x	
Assess concomitant medication use[c]	x	X	x	x	x	x	x
Investigational product dispensed[c]	x		x	x	x		

Conclusions

- This trial has the potential to demonstrate that a reduced dose of apixaban does not increase the risk of VTE recurrence while decreasing the risk of bleeding.
- This result, if achieved, will further improve the therapeutic approach to cancer patients with VTE, making it completely comparable to that of patients without cancer, with enormous advantages in terms of compliance and quality of life.